Status of the Claims

Claims 1-4, 9-14 and 19 have been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. New Claims 20 and 21 are presented. Support for the newly presented Claims can be found generally throughout the Specification.

The Double Patenting Rejection

In the Office Action mailed March 16, 1999 with respect to the instant Application, the Examiner rejected Claim 19 under 35 U.S.C. § 101 as claiming the same invention of that of Claim 1 of prior U.S. Patent No. 5,591,629. Applicants have now amended Claim 19 to remove SCH 94.03 from the Markush group, in an effort to facilitate prosecution. Applicants Claim 19, as amended, does not recite the antibody SCH 94.03 and the Examiner's rejection is now moot. Applicants respectfully request that the 101 rejection be withdrawn.

The Examiner's § 102(b) Rejection

In the Office Action mailed March 16, 1999, the Examiner maintained her rejection of Claims 1-4, 9 and 11-14 under 35 U.S.C. 102(b) as being anticipated by Miller et al (J. Neurosci. 14:6230-6238, 1994). In her original rejection under 102(b) regarding Miller et al (1994) (paper No. 9 dated October 2, 1997) the Examiner remarked that Miller et al teach that administration of the antibody SCH 94.03 was found to promote central nervous system remyelination and therefore inherently treat demyelinating disease in mice infected chronically with Theiler's murine encephalomyelitis virus. Applicants point out that Miller et al 1994, which was published after the date of filing of the priority application (now U.S. Patent No. 5,591,629 (the "'629 Patent")), refers to and discloses data and information with regard to only antibody SCH 94.03 and SCH 94.32. Miller et al 1994 is not suitable or available for a 102(b) rejection as to the antibody SCH 94.03, in view of the earlier filing date of the '629 Patent. Applicants have now amended Claims 1 and 9 to remove SCH 94.03 from the Markush group and present new Claims 20 and 21 wherein methods comprising administering antibody SCH 94.03 of the original Markush group have been separately claimed. Applicants

further submit that the Miller et al 1994 publication does not explicitly describe or teach the particular and specific use of the antibodies 01, 04, A2B5 or HNK-1 (and does not explicitly describe the use of other isolated or synthetic antibodies) in the methods and pharmaceutical compositions.

In further regard to this 102(b) rejection, the Examiner alleges a lack of written description support in the Specification of the priority document (U.S. Patent 5, 591,629) for the use of antibodies 04, A2B5, 01, HNK-1, and isolated or synthetic autoantibodies in the methods and pharmaceutical compositions claimed. Applicants submit, as noted above, that the application of Miller et al 1994 in a 102(b) rejection over the use of antibodies 01, 04, A2B5, HNK-1 and isolated or synthetic autoantibodies in the methods and compositions claimed is improper, in as much as Miller et al does not explicitly teach these antibodies and their specific and particular use in the claimed methods and compositions. Any mere suggestion in Miller et al that SCH 94.03 and SCH 94.32 may be autoantibodies is not a teaching of this now recognized fact. It is important to note that, while not taught in the Miller et al 1994 reference published October, 1994, the identification of SCH 94.03 and SCH 94.32 as autoantibodies and the teaching and description that other such autoantibodies may exist and be capable of stimulating remyelination is present in the '629 Patent - filed April 29, 1994, before publication of Miller et al 1994. In particular, the '629 Patent states at column 11, lines 31-34:

> Thus, it is reasonable to predict that autoantibodies, such as SCH 94.03, play a critical role in stopping an immune-mediated process of demyelination in CNS diseases.

In view of the foregoing remarks and amendments, Applicants respectfully request that the rejection under 35 U.S.C. 102(b) as anticipated by Miller et al 1994 be withdrawn.

The Specification Enables the Claimed Invention

The Examiner has rejected claims 1-4, 9-14 and 19 under 35 U.S.C. 112, first paragraph alleging that "the specification, while being enabled for methods of stimulating remyelination or treating a demyelinating disease in a mammal by administering to a mammal

an effective amount of the monoclonal antibody A2B5, it does not reasonably provide enablement for isolated or synthetic autoantibodies or treatment of a demyelinating disease in mice or humans."

With regard to this rejection, the Examiner first asserts that Applicants have not established the unrestricted public availability of 01, 04 and HNK-1 antibodies. Applicants submit that the 01, 04 and HNK-1 antibodies are publicly available. To further establish the public commercial availability of HNK-1, Applicants have identified three companies, Leinco Technologies, Research Diagnostics, Inc., and Becton Dickinson Immunocytochemistry Systems that are offering HNK-1 antibodies for sale as indicated by their web sites. Copies of the materials offering HNK-1 (anti-CD57) antibody for sale by Leinco Technologies, and Research Diagnostics, Inc. and Becton DIckinson Immunocytochemistry Systems are attached as Exhibit A, B and C, respectfully. Applicants also point out that the ATCC worldwide web site record regarding HNK-1 antibody indicates distribution of the antibody by Becton Dickinson Immunocytochemistry Systems, Biomeda Corp., and Progen Biotechnik GmbH (attached as Exhibit D). To establish the public availability of the 01 and 04 antibodies, Applicants have identified thirty-one (31) research abstracts for scientific studies using 01 and/or 04 antibodies from nineteen (19) different laboratories worldwide between 1981 and 1999 (attached as Exhibit E). Applicants submit that the attached demonstrates that 01 and 04 antibodies have been made available to the public, on a worldwide basis, for the past eighteen (18) years. In addition, antibodies 01 and 04 are being publicly advertised as available for sale by Roche Molecular Biochemicals USA (Exhibit F). The 01 and 04 antibodies listed from Roche Molecular Biochemicals are identical to the 01 and 04 antibodies used by Applicants. Antibody 04 is also available commercially from Chemicon International (Exhibit G). Applicants assert that the 01, 04 and HNK-1 antibodies are indeed publicly available on an unrestricted basis and that the enablement requirement has been met.

In further regard to the 112, first paragraph rejection, the Examiner maintains that polyclonal antibodies such as isolated or synthetic autoantibodies are not enabled by the Specification. Applicants do note, however, that the Examiner does state that the scope of Claims 1-4, 9-14 and 19 for antibodies SCH 94.03, SCH 97.08, 01, 04, A2B2, HNK-1, and

antigen binding fragments thereof are enabled, provided that the deposit issues are appropriately settled. Applicant's submit that the arguments and evidence set forth above with regard to the deposit issues appropriately addresses and overcomes the 112, first paragraph +rejection based on public availability. Applicants now assert that the scope of Claims 1-4, 9-14 and 19 for antibodies SCH 94.03, SCH 97.08, 01, 04, A2B2, HNK-1 and antigen binding fragments thereof are fully enabled.

With regard to the Examiner's position that isolated or synthetic autoantibodies capable of stimulating remyelination are not supported, Applicants respectfully disagree. The skilled artisan can readily make or derive isolated or synthetic autoantibodies (whether polyclonal or monoclonal) with the characteristic of being capable of inducing remyelination of central nervous system axons, as claimed, using conventional methods known to the skilled artisan, including those disclosed in the Specification. In support of this, Applicants attach hereto a copy of a submitted publication detailing research studies completed by individuals, including inventor Moses Rodriguez, entitled "Human Antibodies Promote Remyelination of Spinal Cord Lesions in a Model of Multiple Sclerosis" (attached as Exhibit H). The attached manuscript describes the isolation and characterization of human antibodies (polyclonal IgM antibodies and monoclonal antibodies) that promote remyelination in a viral model of multiple sclerosis, specifically an *in vivo* mouse model of Theiler's murine encephalomyelitis virus (TMEV)-induced demyelination. The results on the attached manuscript describe the following: (a) isolated polyclonal human IgM stimulates remyelination in the spinal cords of TMEV-infected mice and (b) isolated human monoclonal antibodies stimulate remyelination in the spinal cords of TMEV-infected mice. Numerous human monoclonal antibodies were isolated. Importantly, these antibodies were isolated from different individuals (humans), with distinct pathological conditions, if any. Sequencing of the heavy chain and light chain variable regions of two of the human monoclonal antibodies, SHIgm22 and ebv HIgm MSI19010, as shown in Figure 6, demonstrated that they closely match human germline sequence, with SHIgm22 being nearly identical to germline, a characteristic of autoantibodies. Both of these isolated human monoclonal antibodies are shown to stimulate remyelination (as depicted in Table I). These results demonstrate that human polyclonal or monoclonal autoantibodies, capable of

inducing remyelination, can be isolated or made using conventional methodology known to the skilled artisan, even as of the earliest priority date (April 29, 1994). Sequences determined from these isolated antibodies (as shown in Figure 6), can be utilized by the skilled artisan in generating and testing synthetic antibodies using methods and tests known in the art, including as provided in the Specification. In conclusion, Applicants submit that isolated or synthetic autoantibodies which are capable of stimulating remyelination are enabled by the Specification and can be made or derived by the skilled artisan, using conventional methods.

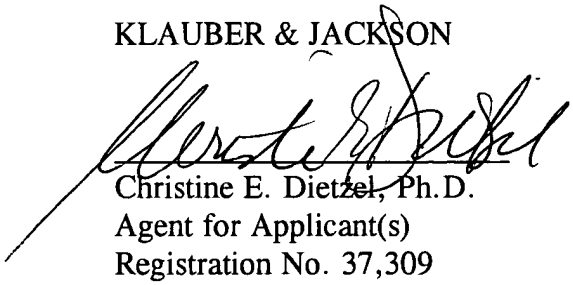
In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C. 112, first paragraph is overcome and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The claims as amended are believed to be in condition for allowance. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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